World Cancer Research Journal WCRJ 2021; 8: e2119

HIGH DIETARY ACID LOAD IS ASSOCIATED WITH PROSTATE CANCER RISK: AN EPIDEMIOLOGICAL STUDY.

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Abstract – *Objective:* *Dietary acid load contributes to metabolic acidosis, which leads to inflammation and cell transformation, closely linked to cancer development. The epidemiologic evidence associating diet-dependent acid load and cancer risk, particularly for prostate cancer, is severely limited, based on a single study. Therefore, we sought to explore this association in the present study.*

Patients and Methods: *A case-control study was performed in 1292 patients (323 cases and 969 age-frequency and urban/rural residence matched controls), through a multi-topic inquiry including a food frequency questionnaire. Food-derived nutrients were calculated from available databases. Dietary acid load was calculated based on two validated measures (Potential Renal Acid Load score and Net Endogenous Acid Production score). Odds ratios and their 95% confidence intervals were estimated by logistic regression, adjusting for potential confounders.*

Results: *We found direct associations between dietary acid load and prostate cancer risk. Both acid load scores were significantly associated with an increased prostate cancer risk (odds ratios =1.56 and =1.81 for highest Potential Renal Acid Load and Net Endogenous Acid Production, respectively). Linear trends were found in both risk estimates.*

Conclusions: *A high dietary acid load may contribute to prostate cancer development. Both acid load scores were directly associated with animal-based foods (mainly meat) intake, and inversely associated with plant-based foods intake. Our findings are consistent with previous studies associating certain dietary patterns with an increased prostate cancer risk. However, further research is warranted to confirm the present findings.*

KEYWORDS: *Acid load, Diet, NEAP, PRAL, Prostate cancer.*

LIST OF ABBREVIATIONS: *BMI = body mass index; CI = confidence interval; FFQ = food frequency questionnaire; NEAP = Net Endogenous Acid Production; OR = odds ratio; PC = prostate cancer; PRAL = Potential Renal Acid Load; SD = standard deviation.*

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INTRODUCTION

Prostate cancer (PC) is one of the leading malignancies among men worldwide [1]. In 2020, more than 1.400.000 new cases were diagnosed, and more than 375.000 men died of PC worldwide[1]. Several non-modifiable risk factors, including age, ethnicity, and history of PC, have been implicated in the development of the disease[2]. Recent studies shifted attention toward modifiable risk factors and emphasized a potential role of diet and lifestyle factors in the development and progression of PC[2,3]. A high meat and dairy intake were repeatedly shown to correlate with an increased total PC risk[4,5]. In contrast, plant-based dietary patterns showed a statistically significant protective association with PC risk[6].

Dietary acid load and its association with the risk of cancer is a rapidly emerging area of high epidemiological interest. Nowadays, it is widely accepted that nutritional factors influence the plasma acid-base equilibrium in the human body[7]. A diet rich in sulfur-containing amino acids, which are readily found in meats, eggs and dairy products, is considered net-acid producing[7,8]. In contrast, most vegetables and fruits are net-base producing foods[8]. Therefore, an acidogenic diet is determined by the balance between base and net-acid-forming dietary constituents[8].

Consumption of a chronic acidogenic diet may induce 'low-grade' or 'chronic metabolic acidosis' in humans, with blood pH levels in the near lower physiological range[8]. This low-grade metabolic acidosis state is considered a type of systemic stress[8] and was associated with the development of severe metabolic alterations that are potentially cancer-promoting[8,9].

Current epidemiologic evidence emphasizes a potential association between diet-dependent acid load and large bowel[10], breast[11,12], lung[13], and pancreatic cancer[14]. However, little is known about dietary acid load and its potential role in PC[15]. Thus, we sought to investigate the potential associations based on a multisite epidemiologic research project in Uruguay. This is a developing country; however, it has a high human development index[16]. Local diets are meat-based and the country has the highest per capita beef intake worldwide[17]. Yet, PC incidence rate in Uruguayan men is similar to many South European countries[1]. To the best of our knowledge, the present epidemiologic study on dietary acid load and PC is the first one in a Western cohort.

PATIENTS AND METHODS

Selection of cases and controls

In the context of a multicentric epidemiological study (1994-2000), we identified all recently diagnosed and confirmed diagnoses of PC. Cases were obtained from 4 large public hospitals in Montevideo, the capital of Uruguay. The hospitals included the Oncology Institute, Pasteur, Maciel, and the Clinicas University Hospital. A high number of patients coming from the public healthcare system are admitted to those institutions, to diagnose and/or treat cancer. Montevideo centralizes approximately 50% of the incident cancer cases. During the study period, 335 PC cases were identified. Eight patients did not consent to the interview (response rate: 97.6%). Another four failed to complete the food frequency questionnaire (FFQ), finally yielding 323 cases. Back in those years, PC screening was non-existent in Uruguay, thus, most diagnosed cases should be considered advanced ones.

All men admitted to the same institutions (during the same time frame) for diseases unrelated to alcohol or tobacco abuse were eligible to participate in the study. We excluded those with recent dietary modifications. Nine hundred and ninety-nine (998) patients were selected and the interview was refused by twenty-nine (29) of them (response ratio 97.1%). Nine hundred sixty nine (969) patients completed the questionnaire and were included in our study as controls, who were matched to cases on age-frequency (10-year categories), region (Montevideo/Other), and urban/rural residence. The following was the classification of controls: eye disorders (254, 27.3%), abdominal hernia (232 patients, 25.0%), skin diseases (88, 9.5%), injuries and trauma (66, 7.1%), appendicitis (62, 6.6%), varicose veins (51, 5.5%), hydatid cyst (47, 5.1%), bone diseases (45, 4.9%), blood disorders (40, 4.3%), and other medical disorders (44, 4.7%).

In a first step, trained social workers who were unaware of the research goals undertook regular screenings to identify recently diagnosed PC patients. Afterwards, potentially eligible patients and controls were contacted by the interviewers. After consenting to the trial, all subjects were face-to-face interviewed. We did not accept proxy interviews. Patients admitted to public medical centers usually had low incomes and were granted free access to health services, (based on Uruguayan law). No individuals were excluded as outliers for any dietary component.

Each hospital director authorized the project after obtaining approval from the respective Ethical Committee. Back then, only oral consent

patient was required, assuming their data confidentiality. To preserve anonymity, we built an auto-generated number, based on family names and ID number.

Questionnaire

The questionnaire included socio-demographic and anthropometric parameters, current occupation, cancer history in 1st-2nd degree relatives; self-reported height and weight five years before the interview; alcohol and smoking status, amount and duration; a history of tea, coffee and "mate" infusions; and finally, a 64 items FFQ, representative of the Uruguayan diet. We focused on food consumption five years before the interview. The FFQ was not validated, but tested for reproducibility[18], allowing the estimation of individual energy intake. All dietary questions were open-ended. Local tables of food composition were used to estimate energy and nutrient intake[19].

Smoking history covered the following points: smoking status; tobacco type; manufacturing type; start and cease ages; smoking duration; intensity, measured in pack-years (total calculated 20-unit packs smoked per day × years of smoking duration). Patients who abandoned smoking during the year before the interview were entered as current smokers.

Estimation of dietary acid load

We calculated diet-dependent acid load using previously reported formulas[20,21] and employed in some of our recent epidemiological trails investigating the relationship between cancer risk and dietary acid load[10,12,13]: net endogenous acid production (NEAP) and potential renal acid load (PRAL). These measures were calculated as follows:

$$\text{NEAP (mEq/day)} = (54.5 \times \text{protein[g/day]}) / (0.0256 \times \text{potassium[mg/day]}) - 10.2$$

$$\text{PRAL (mEq/day)} = (0.49 \times \text{total protein [g/day]}) + (0.037 \times \text{phosphorus[mg/day]}) - (0.021 \times \text{potassium[mg/day]}) - (0.026 \times \text{magnesium[mg/day]}) - (0.013 \times \text{calcium[mg/day]}).$$

The PRAL score includes intestinal absorption rates for the following micronutrients: potassium, phosphate, magnesium, calcium and protein. Previous studies validated the PRAL score *vs.* in urinary pH in healthy individuals [20]. The NEAP score considers sulfuric acid production due to protein metabolism and the rate of bicarbonate production from metabolism of intestinally absorbed potassium salts of organic acids are central (yet highly variable) components of the NEAP score[21]. Both scores were strongly correlated ($r=0.84$, $p< 0.001$) in previous studies. A negative NEAP or PRAL value indicates an alkaline-forming potential, whereas a positive value indicates an acid-forming potential.

Estimation of iron and nutrients intake

Energy intake -the sum of all individual values- was calculated with an analysis program. Values were calculated after multiplying the amount of servings per year by the ratio serving calories/100g of each, divided by 365 days. Serving sizes of solid foods were usually between 100-150 g. Iron intake is highly correlated with energy, therefore, we calculated iron density (daily mg of each mineral/kcal × 1000). Iron intakes were estimated based on previous studies and by applying our FFQ[10,12,13].

Statistical analysis

Most questionnaire variables were continuous, but, if necessary, were categorized into tertiles or quartiles for analysis purposes. Selected variables were entered into the regression models after univariate analyses. In order to make comparisons, those variables were tabulated as mean +/- standard deviation (SD). The association between PC and exposure levels of PRAL and NEAP were estimated by unconditional logistic regression with their odds ratios (ORs) and 95% confidence intervals (95% IC)[22]. Reported *p*-values were two-sided, and associations with *p*-values<0.05 were considered statistically significant. The multivariate analyses included potential confounders.

Regression models included the following independent variables: age (continuous), residence (urban/rural), education years (continuous), Body Mass Index (BMI, continuous), family history of cancer in 1st- and 2nd-degree relatives (categorical, 3), alcohol status (categorical, 3), alcohol duration (continuous), smoking status (categorical, 3), smoking intensity (pack-years, categorical, 4), "mate" intake (liters/day, categorical, 4), and intakes of energy (continuous), α-carotene (continuous), β-carotene (continuous), lignans (continuous), flavonols (continuous), glutathione (continuous), vitamin C (continuous), and total heterocyclic amines (HCA, categorical, 3). We used STATA software (Release 10, Stata Corp LP, College Station, TX, USA; 2007) for all calculations.

RESULTS

Table 1 displays the distribution of both controls and cases based on selective variables. The study design yielded residence (urban/rural status) and age distribution with similar proportions. Although participants were not perfectly matched, non-significant differences were achieved with regard to residence regions (p=0.80). We found no significant intergroup differences with regard to education. In comparison to controls, cases had a higher body mass index, a higher family history of cancer rate, and higher "mate" intake. No statistical differences were found with regard to red meat, processed meat, or plant food intake. Of note, the proportion of individuals consuming alcohol, smoking cigarettes and drinking tea was lower among cases.

Table 2 presents selected nutritional variables, which were analyzed as mean values ± SD. Controls had higher mean intakes of total fiber, flavonols, and vitamin E, (despite lacking statistical

TABLE 1. Selected socio-demographic characteristics, and dietary features of the population under study (n=1292). Distribution of cases and controls.

Variables	*Categories*	*Controls*		*Cases*		*Global p-value*
		(n=969)	*%*	*(n=323)*	*%*	
Age groups	≤ 50	9	0.9	3	0.9	
	50-59	64	6.6	18	5.6	
	60-69	318	32.8	106	32.8	
	70-79	486	50.1	162	50.1	
	80-89	92	9.5	34	10.5	0.96
Urban/Rural status	Urban	690	71.2	230	71.2	
	Rural	279	28.8	93	28.8	1.00
Residence Regions	Montevideo	485	50.0	159	49.2	
	Other counties	484	50.0	164	50.8	0.80
Education years	≤ 2	315	32.5	104	32.2	
	3-4	309	31.9	107	33.1	
	≥ 5	345	35.6	112	34.7	0.91
Body Mass Index (kg/m²)	≤ 24.04	346	35.7	85	26.3	
	24.05-26.38	323	33.3	109	33.7	
	≥ 26.39	300	31.0	129	39.9	0.002
F.H. of cancer in 1st & 2nd degree	No	694	71.6	216	66.9	
	1	220	22.7	76	23.5	
	≥2	55	5.7	31	9.6	0.04
Tea status	Never	760	78.4	287	88.9	
	Ever drinker	209	21.6	36	11.1	<0.001
"Mate" intake	Never	121	12.5	31	9.6	
	<1 l/day	219	22.6	56	17.3	
	≥ 1 l/day	629	64.9	236	76.1	0.03
Red meat intake (serv/year)	≤ 365	566	58.4	179	55.4	
	≥ 366	403	41.6	144	44.6	0.35
Processed meat (serv/year)	≤ 100	482	49.7	155	48.0	
	≥ 101	487	50.3	168	52.0	0.58
Plant foods intake (serv/year)	≤ 934	320	33.0	120	35.0	
	935-1426	320	33.0	109	33.7	
	≥ 1427	329	34.0	101	31.3	0.66
Dietary energy (kcal/day)	≤ 1578	318	32.8	114	35.3	
	1579-2042	327	33.8	103	31.9	
	≥ 2043	324	33.4	106	32.8	0.70
Alcohol status	Never	282	29.1	131	40.5	
	Ex drinker	167	17.2	91	28.2	
	Current	520	53.7	101	31.3	< 0.001
Smoking status	Never	190	19.6	86	26.6	
	Ex smoker	422	43.6	144	44.6	
	Current	357	36.8	93	28.8	0.006
Total patients		969	100.0	323	100.0	

Abbreviations: FH of Cancer = family history of cancer.

TABLE 2. Mean daily values ± standard deviation of selected nutrients and bioactive substances adjusted by energy. Comparison between cases and controls.

Variable	*Units*	*Controls Mean ± SD*	*Cases Mean ± SD*	*Diff.(p-value)*
Energy	Kcal	1857 ± 568	1820 ± 513	0.30
Total fibre	g/10³ Kcal	6.62 ± 2.58	6.33 ± 2.34	0.08
Heme iron	mg/10³ Kcal	2.33 ± 0.84	2.43 ± 0.86	0.06
NHeme iron	mg/10³ Kcal	8.30 ± 1.87	8.30 ± 1.82	0.98
Total HCA	ng/10³ Kcal	16.22 ± 6.20	17.16 ± 6.46	0.02
Carotenoids	µg/10³ Kcal	6.21 ± 4.08	6.29 ± 3.81	0.76
Flavonols	mg/10³ Kcal	1.93 ± 1.65	1.78 ± 1.52	0.16
Lignans	µg/10³ Kcal	1802 ± 547	1798 ± 533	0.92
Animal gsh	mg/10³ Kcal	9.74 ± 3.19	10.16 ± 3.23	0.04
Plant gsh	mg/10³ Kcal	11.21 ± 4.85	10.92 ± 4.29	0.34
Vitamin C	mg	62.7 ± 43.1	60.5 ± 42.6	0.42
Vitamin E	mg	3.83 ± 1.47	3.67 ± 1.23	0.07

Abbreviations: g = grams; mg = milligrams; ng = nanograms; µg = micrograms; Gsh = glutathione; HCA = heterocyclic amines.

significance), whereas cases displayed higher intakes of HCA, heme iron, and animal-based glutathione. Ultimately, no differences were observed for energy, non-heme iron, carotenoids, vitamin C, plant-based glutathione and lignans.

Table 3 shows both acid load scores (PRAL and NEAP) as well as their original components. Scores are higher in cases than in controls. Neither the studied global minerals nor those with animal/plant sources differed statistically between cases and controls.

Table 4 displays the adjusted ORs for both acid load scores. The highest *vs.* lowest tertile of PRAL derived a significant estimate (OR=1.52, 95% CI 1.01-2.28, p_{trend} = 0.001) with a highly significant trend (p_{trend} = 0.001). The same applies to the NEAP score: both risk and trend estimates were significant (OR=1.72, 95% CI 1.16-2.48, p_{trend} <0.05). These scores were obtained using the most demanding model, which included selected antioxidants (**α**-carotene, **β**-carotene) and pro-carcinogenic compounds (HCA). The regression models

TABLE 3. Mean daily values ± standard error of the acid load scores and their components. Stratification of items according to their animal/plant original source. Comparison between cases and controls.

Variable	*Units*	*Controls Mean ± SD*	*Cases Mean ± SD*	*Diff.(p)*
Total Proteins	g/d	54.6 ± 19.9	55.5 ± 20.3	0.49
Animal proteins	g/d	49.6 ± 19.3	50.6 ± 19.6	0.44
Plant proteins	g/d	4.9 ± 2.2	4.9 ± 2.3	0.64
Total Phosphorus	mg/d	785.9 ± 252.1	784.9 ± 246.4	0.95
Animal phosphorus	mg/d	465.3 ± 182.5	482.0 ± 194.1	0.16
Plant phosphorus	mg/d	320.6 ± 132.7	302.9 ± 117.3	0.03
Total Potassium	mg/d	1952.5 ± 652.9	1926.1 ± 639.5	0.53
Animal potassium	mg/d	661.3 ± 265.6	683.1 ± 280.6	0.21
Plant potassium	mg/d	1291.2 ± 537.6	1243.0 ± 527.2	0.16
Total Magnesium	mg/d	182.3 ± 61.7	177.7 ± 58.3	0.24
Animal magnesium	mg/d	51.8 ± 20.4	53.6 ± 21.5	0.15
Plant magnesium	mg/d	130.6 ± 53.3	124.1 ± 50.1	0.055
Total Calcium	mg/d	600.3 ± 263.2	578.2 ± 211.9	0.17
Animal calcium	mg/d	350.8 ± 229.7	337.6 ± 182.7	0.35
Plant calcium	mg/d	249.5 ± 98.6	240.5 ± 86.3	0.15
PRAL score	mEq/d	2.29 ± 0.35	3.65 ± 0.65	0.06
NEAP score	mEq/d	51.2 ± 0.60	52.5 ± 0.92	0.27

TABLE 4. Crude and Adjusted Odds Ratios (OR) of PC for acid load scores (PRAL and NEAP).

	I		II		III		
	OR	95% CI	OR	95% CI	OR	95% CI	Trend (p)
PRAL (mEq/d)	**≤ -1.13**		**-1.12 - 6.75**		**≥ 6.76**		
Model 1	1.00	---	1.11	0.81-1.52	1.22	0.89-1.66	0.22
Model 2	1.00	---	1.18	0.85-1.64	1.38	0.99-1.93	0.06
Model 3	1.00	---	1.28	0.90-1.83	1.52	1.01-2.28	0.001
NEAP (mEq/d)	**≤ 43.1**		**43.2 - 57.0**		**≥ 57.1**		
Model 1	1.00	---	1.34	0.98-1.83	1.31	0.96-1.80	0.09
Model 2	1.00	---	1.46	1.12-2.23	1.52	1.18-2.51	0.015
Model 3	1.00	---	1.58	1.10-2.18	1.72	1.16-2.48	0.048

Regression models:
Model 1 = Adjusted by age (continuous) and residence (urban/rural)
Model 2 = Model 1 + family history of cancer (categorical, 3) + education (continuous) + smoking status (categorical, 3) + smoking intensity (categorical, 4) + alcohol status (categorical, 3) + alcohol drinking duration (continuous) + "mate" intake/day (categorical, 4) + body mass index (continuous) + energy (continuous)
Model 3 = Model 2 + α-carotene (continuous) + β-carotene (continuous) + total HCA (categorical, 3)

analyzing both acid load scores were compared using a term for energy as a continuous and as a categorical variable, and OR estimates were very similar (variations within 1-2%, data not shown).

Additional stratified analyses were done based on family history of cancer, BMI, and iron intakes, but with null results (data not shown).

DISCUSSION

This epidemiological investigation revealed direct associations between a high dietary acid load and PC risk. However, those associations were stronger for the NEAP score compared to those of PRAL score and varied depending on the employed scoring methods and regression models.

Only one previous case-control study on dietary acid load and PC risk was carried out[15]. Albeit these authors analyzed a very small sample of Iranian men (60 cases and 60 controls), a larger FFQ was employed. Our results coincide with this recent study, regarding the higher adjusted NEAP score compared to the adjusted PRAL score: we obtained an OR=1.72 *vs.* 1.52, respectively, and the quoted authors obtained an OR=3.88 *vs.* 3.42, respectively. The different estimates might reflect differences of employed regression models. As an example, dietary iron was included in the analyses because, in our previous epidemiologic studies on dietary acid load and cancer, it has shown a role for cancer risk[10,12,13]. Nevertheless, this was not the case for the present study.

Dietary intake is an important environmental factor that may drive the development or maintenance of cancer, most probably through epigenetic modifications[8]. On the other hand, reviewing potential pathophysiological pathways, no studies showed a direct link between dietary-induced acidosis and the development of cancer[8]. In this respect, diets high in PRAL induce a low-grade metabolic acidosis state that has been associated with detrimental metabolic alterations and adverse clinical conditions[8,9].

One example is enhanced glucocorticoid secretion triggered by metabolic acidosis[23]. Potentially acidogenic diets high in protein lead to a significantly increased cortisol production in humans[8,23]. Although short-term studies showed diet-induced acidosis to be generally mild (and subsequent increased cortisol activity within the normal range), it is not inconceivable that a chronic acidogenic diet may lead to pathophysiological consequences in the long run.

Upregulated cortisol bioactivity, subsequent to diet-induced metabolic acidosis, may promote reduced insulin sensitivity and increased insulin resistance[24]. The latter is a hallmark of diabetes, which has, in turn, been associated with the development of PC[25]. Acidosis-induced insulin resistance also results in compensatory pancreatic insulin secretion and hyperinsulinemia[8], which has likewise been associated with the development, progression, and aggressiveness of PC[26].

Moreover, long-term consumption of potentially acidogenic high protein diets was correlated with higher insulin growth factor (IGF-1) serum levels[8]. The European Prospective Investigation into Cancer and Nutrition revealed that IGF-1 levels were positively related to protein and milk intake, while an inverse relation with vegetables was found[27]. These points warrant further investigation, as the IGF axis plays a remarkable role in PC etiology and progression[28].

Another potential link between acidogenic diets and PC is adiponectin [8]. Adiponectin is an adipokine hormone that enhances insulin sensitivity and possesses anti-inflammatory and anti-atherogenic properties[29]. Low serum adiponectin levels are considered to be permissive for cancer development[8]. In metabolic acidosis, circulating adiponectin is lowered through inhibition of adiponectin gene transcription in adipocytes[29]. Thus, it is reasonable that a chronic acidogenic diet could potentially increase PC risk by negatively affecting adiponectin serum levels.

A diet-induced acid-base imbalance may affect several molecular and cellular activities which can stimulate carcinogenesis or induce tumor progression[11]. A recent study revealed an association between a higher invasive breast cancer risk and a higher PRAL score[11]. While comparable studies in PC patients are scarce, it seems reasonable that the same association applies to this cohort of patients as well. El-Kenawi et al[30] recently demonstrated that tumor acidity contributes to prostate carcinogenesis by altering the state of macrophage activation. While malignant cells already contribute to the increased pericellular accumulation of organic acids (e.g. lactic acid) due to the 'Warburg Effect'[30], it might be even more detrimental to reinforce this with an acid-producing diet rich in meat, fish, and dairy products.

Recently, the gut microbiota was reported as a producer of various metabolites that can contribute to carcinogenesis in the immediate area and even in distant organs through their absorption and systemic circulation from the gut[31]. A gut dysbiosis leads to low-grade chronic inflammation. It has been linked to several distant cancers, perhaps involving the production of superoxide radicals, growth factors, and bacterial genotoxins, too[32]. Anyway, its role in PC is still controversial: certain bacterial and functional features within gut microbiota composition are associated with PC risk, however, a majority of the PC studies, including microbiological aspects, have investigated either prostate tissue or urinary tract microbiota with conflicting results[32]. There is still a knowledge gap between changes in the microbiome due to diet and long-term consequences, such as cancer development, but microbes are considered as potential key mediators in diet–cancer interactions. In this sense, for example, an optimal iron homeostasis is critical for regulation of host immunity and metabolism in addition to regulation of commensal and pathogenic enteric bacteria[33]. This reason and some of our findings related to dietary iron and cancer epidemiological risk[34-36] motivated us also to explore a possible role for iron in the current study, without positive results.

Interestingly, studies have demonstrated variable sodium/potassium ratio effects on microbe diversity based on geographical location (environment). It suggests that the quoted mineral consumption -which is part of the studied items in the present study- plays a variable role in regulating the abundance of pathogenic microbes[37]. These facts add complexity to the picture, indeed.

Our study has strengths and weaknesses that warrant further discussion. The interview of participants was done face-to-face by the same interviewers at the same institutions. The population sample was comprehensive from the viewpoint of country areas and socio-economic subsets. Data collection was performed during the same period.

The high participation rate of identified cases and controls (rates ~97%), favored by the interview during the hospital stay, limited possible selection bias. Dietary habits were relatively stable in Uruguay, and participants were instructed to report any relevant dietary modifications occurring during their life**.** Furthermore, a recall bias (with regard to nutritional habits) is unlikely in the examined population, as the awareness of PC's dietary hypothesis was inexistent

A limitation of our trial is the non-validated FFQ, yet, it was satisfactorily reproducible[18]. The validation was projected to be done, but due to external factors in the early 2000s, it was not performed later. Potential confounders, such as occupational and home exposure to smoking and other kinds of pollution, are potential limitations of our research and were not assessed in present study, as it was based on average serving sizes rather than actual food sizes. Mineral content in water, other constituents of animal foods, and the effects of different cooking methods might play a role of potential confounders which cannot be excluded.

CONCLUSIONS

The calculated NEAP and PRAL scores were found to be directly and significantly associated with PC risk, in both cases supported by more complex regression models. High PRAL and NEAP scores were associated with high meat consumption, whereas low PRAL and NEAP scores were associated with the consumption of plant foods. Thus, our results indicated that an acidogenic dietary pattern may have contributed to the increased PC risk in the examined population. Our results are in agreement with previous studies focusing on food groups, dietary patterns and PC risk. Albeit they may increase this risk, further investigations are warranted to confirm these findings.

Acknowledgment:
No financial support was received for the current research.

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Conflict of interest:
There is no conflict of interest to be declared by the authors.

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